

Atty Dkt. No.: PT2087000  
USSN:10/771,383

### REMARKS

#### FORMAL MATTERS

No amendments have been made to any part of the application.

#### REJECTIONS UNDER § 103(A)

The Examiner has restated their rejection of the claims presently on file in view of Lin *et al.* The Examiner alleges that Applicants' previous arguments are not persuasive "because of the open claim language comprising encompasses the scope of the full invention." Furthermore, the Examiner alleges that the unexpected advantages over the prior art set out by the Applicant are merely an allegation lacking factual support. Applicant respectfully disagrees and submits that the Examiner has not provided a *prima facie* case of obviousness and that Examples 1 to 3 of the present application clearly provide factual evidence of record that support the unexpected advantages offered by the processes set out in the claims of the present application.

Lin *et al.* does not disclose step (b) of independent claims 1 and 23 of the present application. More particularly, Lin *et al.* does not disclose adding atorvastatin sodium salt to an aqueous calcium chloride or calcium acetate solution. As such a *prima facie* case of obviousness has not been presented by the Examiner.

Paragraph [0016] of the present application as originally filed states:

Surprisingly, contrary to WO 02/083638, we have discovered that the order of addition in step (b) is important in terms of the morphology of the resulting amorphous atorvastatin calcium. The order of addition in step (b) as per the present invention results in isolation of a product, which is significantly easier to filter and dry. Furthermore, the filter cake obtained when following the procedure of the present invention retains less residual water relative to the standard mode of addition. For instance, the water content of the filter cake using the conventional order of addition is about 10%

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to 20% higher relative to the present invention. These differences are of importance when transiting to larger scale manufacture of amorphous atorvastatin calcium salt.

Example 1 of the present application involves adding to an atorvastatin sodium salt solution a Calcium Chloride solution. This is the same order as set out in Lin *et al.* (column 5, lines 28 of Lin *et al.* states "To this solution [atorvastatin sodium salt solution] is added a solution of calcium acetate hemihydrate" (emphasis added)). Examples 2 and 3 of the present application involve adding to a calcium chloride solution the atorvastatin sodium salt solution. This is the opposite order of adding the reagents when compared to Example 1 and Lin *et al.* Examples 2 and 3 of the present application clearly show that the combined time required for the filtration and washing steps when carried out under the same filtration and washing conditions as Example 1 is reduced by over 50% in both cases when compared to Example 1 and that the moisture content of the damp filter cake of Examples 2 and 3 are significantly less when compared to Example 1. Examples 1, 2 and 3 of the present application are clear evidence of record that provide factual support of the statements of unexpected advantages over the teachings of the cited art.

The Examiner is respectfully requested to withdraw the rejection and allow the claims.

#### CONCLUSION

The pending claims are believed to satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same is therefore kindly requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided below.

No fees beyond those submitted herewith are believed to be due in connection with this communication. However, the Commissioner is authorized to charge any

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underpayment of fees associated with this communication under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-4648, order number **PT2087000**.

Respectfully submitted,  
APOTEX INC.

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By: 

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